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REMEDIES, OCCASIONED BY SIX
GENERIC CONDITIONS. *Esq*

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HENRY M. FIELD, M. D.

[Reprint from the *Boston Medical and Surgical Journal* of
June 26, and July 3 and 10, 1884.]



CAMBRIDGE:
Printed at the Riverside Press.
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SIX GENERIC DRUG MODIFICATIONS.¹

BY HENRY M. FIELD, M. D.

"I CONCLUDE, therefore, of this and other medicines, as Thucydides of the plague at Athens, no remedy could be prescribed for it, *nam quod uni profuit hoc aliis erat exitio*; there is no catholic medicine to be had, — that which helps one is pernicious to another." — ROBERT BURTON.

WHAT Virchow calls the "mystery of individuality" continually confronts the physician in the prescribing of remedies. Other mysteries may, with growing familiarity, become less obscure; skill and confidence otherwise enlarge with use and experience, but the oldest and the wisest practitioner must still confess himself frequently baffled by the mysterious modifications which the individual constitution continually introduces into the operation of his most familiar remedies. "When," observes a recent writer, "we recall only a few of the minutiae which must be taken into account, for example, the infinitely great difference in the distribution of blood-vessels in organs, the multiform arrangement of glandular tissues in glands, the deviations in innervation of organs, the difference in size of individual nerves, and in the distribution of nerve plexuses, the variations in the gross and in the histological construction of the same muscles in different individuals, we must confess that not only is our present ignorance great, but that it will always continue."

In this connection and of what has been well called anatomical idiosyncrasy, an observation connected with the ophthalmological use of atropia affords a good

¹ Annual Address delivered before the Middlesex South District Medical Society, at Cambridge, April 16, 1884. Published by vote of the Society.

illustration. Instilled into the eye in whatever quantity, employed in collyria for however long a time, atropia should exert no influence beyond its local effect, and such is the general result of its use. There is, however, rarely observed constitutional implication, and this has been traced to an anatomical peculiarity. It is not any part of the salt absorbed from the eye that affects the system, but such portion of it as was taken up by the lachrymal ducts and so conveyed to the throat and stomach. "Susceptibility, therefore, to this mode of action stands in direct ratio to the width of the tear-passages. Proof of this statement is furnished, according to R. Liebreich, by those who have impermeable tear-ducts, and whose general condition is never affected, even by the largest doses used for a long period."¹

Such are but a few, and these the more obvious and superficial, of the conditions which determine individuality. The problem has other elements at once more controlling and recondite, not easily expressed in words, but the reality of which is recognized by every thoughtful physician. "The possibility of explanation," says Virchow, "is no test of knowledge, for we know many things empirically whose causes we cannot comprehend. No exact investigation, either anatomical or physiological, pathological or therapeutical, has ever succeeded in lifting the veil which conceals the conditions governing individual peculiarities. In all times it has been regarded as the peculiar prerogative of exceptionally gifted spirits or of great experience to possess that subtle insight which enables one to recognize, even approximately, the specific character of the individual."

What may be called *indicia* of idiosyncrasy are greatly to be desired; such as past experience has possessed us of are at best few and uncertain. Jonathan Hutchinson has remarked that all persons of dark complexion bear mercurial treatment well and require

¹ Lewin.

larger doses than those who are fair ; nay, more, that individuals of the former class may enjoy better health while taking mercury, “ and are not infrequently much and permanently benefited by a long course.” On the other hand, dark-complexioned people do not bear tonics well, they are apt not to be helped by sea-air ; “ the need of purgatives is greater in them.” In those of fair complexion belladonna is observed to exert its highest power. Just as we know that acne is most liable to appear in individuals of a certain quality of skin and at a certain period of life, so we may expect that the iodides and bromides, pushed a little under these circumstances, will produce characteristic cutaneous eruptions. Finally, we know — and a most unhappy piece of knowledge it often is — that it is just in the constitution which most needs the staying and tranquilizing influence of opium, that is, in the hyperæsthetic and neuralgic female, that its anodyne and hypnotic virtues are most apt to fail us, while in such systems it may play the rôle of a veritable fiend.

The hope that what experience did not impart, an *a priori* method of studying and reasoning might supply, naturally a product of the deductive philosophy of an earlier age, was doubtless directly concerned in the determination of temperaments by the ancients, an effort towards specific knowledge in the direction of individualism. And it must be admitted, though their terms be far from scientific, we all of us still find them very convenient. Indeed, the attempt at classification in individuality has not been wholly resigned to the contemporaries and successors of Galen and Paracelsus ; and it is hardly more than twenty years ago that so prominent a practitioner as Dr. Laycock wrote quite exhaustively upon the subject. It is doubtful, however, if we are made any better off for his six temperaments than for the four we had previously. Such studies have their value in our scientific age, when the minds of men are so generally given to the pursuit of the demonstrable and of that alone which is capable of

strict definition. Once that the disease were determined it is not at all sure that the practitioner trained in the school of Laennec would treat a pneumonia better than would he who was taught in the school of Hippocrates; and quite likely the latter would be nearer right in prognosis. Just here is suggested a danger that we may lose much as medicine makes its transition from art to science. The "gifted spirits" of Virchow are not the anatomists or the pathologists; they are not of necessity the clinicians, full men though they may be, and exact in the practical knowledge of hospitals and schools; they are rather those who, some way, find the largest success in the treatment of disease, whose wide range of therapeutic resources is both intuitive and acquired, whose sense, aided or not by instruments of precision, looks deeper and sees farther than that of other men, who wrest secrets from nature, and, in the language of the French proverb, are concerned "not with sicknesses but with the sick." It was a good pathologist who gave three good reasons why his patient could not get well, but it was a better doctor who, against all reason, rescued him.

The occasional extraordinary behavior of quinine affords a good illustration of what we mean by idiosyncrasy. We do not now refer to what has been called quinine poisoning, a condition which may accrue from quite small doses, and which is variously characterized by determination of blood to the head, œdema of the face, itching of cutaneous surfaces, great excitement, and even delirium, followed by extensive desquamation. This pertains to individuality, but it has been well described in certain cases published in the journals and the books. But in the exceptional condition now in mind quinine acts in a way the exact opposite of its otherwise observed and characteristic action. Intrinsically a corroborant, a dynaphor, as the French conveniently call it, that is, a force-begetting, force-imparting remedy, it now acts to prostrate and overwhelm. The patient complains of increased weariness; there

is trembling of the hands, unsteadiness of gait, a feeling of great weakness in the legs, more or less complete, and perhaps extreme, suffusion of perspiration, with conjoined depression of spirits, melancholy, impaired mental power, etc., etc. Such syndroma, which, in another and otherwise caused, quinia should be calculated directly to antagonize, to relieve or lift altogether, follows so soon after the ingestion of the remedy, and is so surely aggravated by successive doses, that soon, it may well be, both physician and patient are brought to suspect the source of the mischief.¹

A somewhat prevalent misconception or inadequate knowledge among the profession upon the general subject of quinia incompatibility is well illustrated by remarks of Dr. David Young, of Rome, in a recent article contributed to the *Practitioner*. He speaks of a "belief on the part of many patients, a belief also shared in by not a few eminent physicians, that they cannot take quinine in any form or dose; and I have met with such patients in Italy," continues the doctor, "who told me they were advised by their own medical men at home to assure any physician whom they might have occasion to consult that they could not take quinine." He suspects that there is a "physiological reason" for this fact of intolerance, and that "ere long investigation will discover what this reason is," and proceeds to remark upon the "curious fact that the same wide-spread belief exists in regard to the use of iron." The illustration is an unfortunate one; the

¹ I am glad to find, in Hutchinson's Pedigree of Disease, the recognition of a principle which I learned, some time ago, to apply in my own practice, especially in respect of the present material, but which I have not seen stated elsewhere. "It by no means follows," he remarks, "that because a patient has an idiosyncrasy against some drug we ought wholly to abstain from its use. Rather this susceptibility proves, in the majority of cases, that in him minute doses will effect the cure as efficiently as larger ones in others." He instances tertiary syphilitic ulceration cured by one third to one half grain doses iodide potassium. I have applied this method in malarial seizures, and accomplished full medicinal purpose with one half to two grains quinine, and at the same time avoided unfortunate physiological impression.

analogy cannot be maintained, for the fact is, as I conceive it, that iron intolerance, when presented, is, indeed, almost invariably due to a "physiological reason," a temporary physiological condition which it is for the physician to estimate and remove; for example, a state of pyrexia, of biliousness, a failure in selection of the right pharmaceutical preparation, or in determination of the right dose; whereas quinine intolerance, when it exists, is an established fact, and has its source in the very nature of the man, or, in a word, is what we have recognized it to be, a phenomenon of idiosyncrasy.

Iodine, as misdirected by individual constitution, is a not infrequent occasion of surprise, annoyance, or aggravation. For this we may perhaps be partly prepared when we consider the wonderful power of this drug to penetrate the system, the wonderful speed of its circuit, and the extraordinary range of its possible elimination; a threefold quality which may well bring it into collision with a lurking idiosyncrasy. Ingested into the stomach as metalloïd or salt, the promptitude with which it may be rendered in the renal flux or returned in the saliva is familiar to every physiologist. I have, at least on two occasions, had patients to whom I had made application of a few drops tincture iodine, upon absorbent cotton by shielded applicator to the interior of the uterus, declare that iodine had been used because it was tasted in the mouth. Hardly more than three minutes — and surely not five — had elapsed before this impression was made. Here the area of absorption must have been confined to the endometrium, none of the remedy having come in contact with any part of the vaginal wall.

The inherent power which every active remedy has to exert desirable and undesirable properties at the same time is also well illustrated by iodine as modified by individualism. Lewin's experience is here to the point: "Given for the purpose of producing a diminution in volume of hyperplastic glands, as the cervical

lymphatic or the thyroid, etc., it produced the desired effect and at the same time a serious atrophy of glands previously healthy, as the mammae or testicles." Iodine, like opium, may accomplish the purpose of its exhibition, but in so malignant a way that the relief afforded costs seriously through the discomforts it imposes. This is well illustrated by the experience of a patient of mine, a young medical man, who had found in iodide of potassium a complete, and the only effectual, remedy for a painful asthma. The drug, however, produced synchronously such a degree of lachrymal and nasal catarrh, such a persistent foul taste in mouth and foul odor of breath, that the victim of idiosyncrasy, after repeated unfortunate trials, gave up all treatment and resigned himself as patiently as he might to his old enemy.

Iodine is so prolific in individual constitutional disturbances that we leave the subject with reluctance, but can give space for but little further remark. The power which idiosyncrasy, indeed, may assert in this connection is well shown by Hutchinson's observation, who has repeatedly seen doses of only half a grain produce definite symptoms of poisoning in the course of a couple of days; and yet has known a patient to swallow one and a half ounces a day of the best Apothecary Hall iodide for a week together without any especial effect except the production of a degree of lassitude.

The morphology of skin eruptions, under varied constitutional iodism, presents a wide range, and may obtrude problems hard to solve. In one instance an infant was treated for small-pox by "an experienced and sagacious surgeon," and kept carefully quarantined for a month, — to present in the end only a case of iodide of potassium poisoning. A man was treated in hospital for syphilis, pretty surely killed by iodide of potassium, and then declared never to have had syphilis at all. Such experience as this is calculated to enforce the eleventh aphorism of Arnoldus, which asserts that the

"wise and conservative physician never hastens to have recourse to medicine *nisi necessitate cogente*." The misinterpretation which follows has its amusing side. In 1862 the dermatologist Bazin, of Paris, published a description of a new form of skin disease, for which he proposed the name "*hydroa*." Other observers followed with similar accounts. Later, an authority objected both to the term and to the claim of novelty, and pronounced the disease a variety of "*urticaria bullosa*." It was not till some time after 1870 that proof was afforded that all were alike at fault, and in "*hydroa*" was recognized only an extraordinary idiosyncrasic sport of iodine.¹

One illustration more. It has been lately pointed out by a French author that the medicinal employment of the oil of turpentine may occasion a condition of the kidneys which causes the urine, on chemical examination, to simulate albuminuria. This fact is alluded to in my recent monograph on The Balsamiques, and a simple device given by which the error can be set aside. In a volume of papers by Dr. Seguin of New York, — *Opera Minora*, — published the present year, a corresponding charge is brought against iodide of potassium as respects microscopic examination of the urine. He reports three cases attended by conditions which warrant the statement that iodide of potassium "may give rise to the formation of hyaline and epithelial casts without (there being) albuminuria or other rational symptom of Bright's disease." This, so far as I know, is the latest observed — as well as one of the most singular — freaks of idiosyncrasy in the conduct of this versatile drug.

As respects idiosyncrasy in the action of the *alkaline*

¹ Hutchinson remarks of this drug and of its derivatives: "Not even the syphilitic virus itself is capable of producing a greater multiplicity of pathological changes in the integument. Now it is a hemorrhage, now a leucorrhoea, now an erythema, now a bulla, the commonest of all forms is an acne; but in addition to it and to those I have named we may have, at the same time, pustules, lichen-like tubercles, and in aggravated cases, chancres and tubercular growths."

bromides, a closer analogy obtains with what we observe in the drug just discussed than might be expected when we consider difference both of physiological influence and of therapeutical uses. We can devote but one remark to this subject, however. Professor Dühring distinguishes eight varieties of skin disease as characteristic, in different individuals, of bromide saturation, namely, three varieties of acne, a brownish discoloration of the skin, a simple papular eruption, maculo-papules, bullæ, and rupia. To these Dr. Seguin adds a ninth, which he carefully describes, — a semi-malignant looking ulceration upon the lower part of the leg. Of course these results are mostly confined to the practice of neurologists who use maximum doses, as in epilepsy, cerebral tumor, etc.

I might speak of the propensity of chloral hydrate to "fly to the eyes," as it has been called, — and, indeed, shall have a word on this subject a little later, — and this, after moderate and brief use, producing severe conjunctivitis, etc., and, in exceptionally severe cases, photophobia and œdema of surrounding parts; a phenomenon which is now and then observed in less degree from the continued use of the bromides. Carbolic acid appears to be well-nigh controlled by individualism, and to such extent that many writers have questioned whether so powerfully toxic an agent should be used at all, at least to the extent of the production of a perceptible physiological impression.

Here it seems pertinent to introduce the following note: It is generally assumed that idiosyncrasy is a fact both of heredity and transmission, and this is doubtless true; that with various modifications in degree of development, as, for example, an especial prominence at times of weakness or ill-health, it exists as a permanency at least throughout the life of the individual. I have, however, a case at present under observation which shows the actual genesis of an idiosyncrasy *de novo*. My patient is a female of strongly marked neurotic character, made such, indeed, both by inheritance and education.

With strong mind and weak nerves, she affords a prominent illustration of that unhappy type in which there appears to be a more or less constant conflict between what has been called the abdominal and the cerebral brain. Four years ago it became necessary to advise the procuring of sleep by a nightly enema of chloral hydrate, in a moderate dose. This was continued for fully eighteen months without material increase in quantity of the hypnotic. It was then stopped, partly because of the appearance of a mild form of conjunctivitis, and accompanying symptoms. After fully two years' suspension, it recently seemed wise again to resort to this measure, and, accordingly, twenty to thirty grains was ordered by enema on retiring. The therapeutic effect was all that could be desired, but at the end of ten days a summons found the patient in a state of great distress. There were conjunctivitis and photophobia, the eyes were nearly closed by surrounding swelling, the face, suffused, red, hot, presented such a degree of oedema that the husband demanded an examination of the urine before he was satisfied that some disease of the kidneys had not set in. Arrest of the chloral for a few days, and then occasional attempts to return to it, established the fact that the case was idiosyncrasic and due to the remedy employed.

I have spoken of carbolic acid as well-nigh controlled by individualism. Busch regards it as "one of those drugs which indeed act well in medicinal doses, but to which certain persons, for reasons as yet unknown to us, are so sensitive that quantities harmless to innumerable other persons act poisonously upon them;" and Koster has the alarming suggestion that the occasion of the report of so few deaths under antiseptic treatment is to be referred to the uncertainty of the symptomatology of carbolic-acid poisoning, in different constitutions, and hence the casualty "is concealed under the names shock, collapse, and similar terms." The dangers of carbolic-acid spray are noted in another division of this paper. Deaths from the use of this

material, whether as applied to the surface or introduced into the cavities of the body, under conditions which we have no right to say were not cautious and skilled, have taught us that a remedy so capricious is not to be used, except under circumstances of the strictest limitation.

Death from chloroform in competent practice is largely to be referred to idiosyncrasy: "we waste our labor when we search for proof of heart disease or some flaw in the apparatus or some want of care in the administration." Again, says Hutchinson, "It is probable that there are persons in whom, owing to peculiarity of nerve-organization and not in the least to anything we can recognize as ill-health, the inhalation of chloroform will always cause a depression of the heart's action.

A rather startling experience of my own with sulphuric ether the past winter has interest in this connection. The subject was a patient and friend of twelve years' acquaintance, was of middle age, robust health, good habits, had no disease of heart or kidneys. The ether was pure and given in confidence for the extraction of a small tumor of the fore-arm. Hardly had anaesthesia been reached when a sudden and an apparently paralyzing action was exerted upon the respiratory centre, with the production of symptoms which seemed to demand the immediate suspension of the anaesthetic and involved an incomplete performance of the operation intended.

But once again: We do not need to invade the mysteries of the interior of the body in the search for illustrations of our subject; we have but to observe the varied phenomena of medication applied to its surface. The application of the tincture of iodine to the skin should produce only an erythema, but there are subjects with whom it causes vesication and an extensive oedema. Now and then, indeed, it seems impossible to cause any impression, however often it may be applied. But remote and profound constitutional effects may

follow from what was directed for topical external influence alone. Thus Buckell reports that "in the case of a lady, who had the tincture of iodine very lightly painted upon a tumor between the scapulae, there appeared pain and a sense of oppression in the epigastric region and also trembling, weakness, profuse sweating, dribbling of urine, and inability to stand erect. The use of stimulants and application of warmth over the stomach caused these symptoms to disappear in a few days." Here there was wide departure from what should be looked for had even the iodine been administered internally and in toxic dose.

I was called within the year to see a female patient who had believed herself for two days to be suffering from an attack of the measles; but when to an extensive eruption, which showed no disposition to disappear, there were added a degree of blindness, confusion of thought, headache, etc., alarm was taken and the physician called. Almost the first condition noted, after the first general survey, was wide and fixed dilatation of the pupils. Inquiry elicited the fact that the patient had been wearing for several days past a four by six inch perforated belladonna plaster to the small of the back, nor did the subject by any means present the usual type of exceptional susceptibility to belladonna.

But it is not alone in the skin as respects medicines applied to the skin; the phenomena of individualism may be encountered within even narrower limits. An inert ointment made of fresh fat, applied with no extreme degree of friction, will develop inflammation of the cutaneous surface with some subjects, whereas the local phenomena attending the application of a mild oleate of mercury are so varied that it is safe to predict nothing with certainty.

So much for idiopathic idiosyncrasy, which, after all, could probably in every instance be shown to be anatomical as well, as truly as in the instance already cited, could we apply the requisite knowledge in our study of the question. It is anatomical, or rather

physiological, idiosyncrasy which explains certain of the more familiar eccentricities in the behavior of iodide of potassium; the usual rapid, exodic elimination does not obtain; the salt is brought back by the salivary glands, and in the nasal and bronchial mucus, to be re-absorbed or again swallowed, and thus a kind of *vicious circle* is soon set up with attendant coryza, foul breath, foul taste, etc. Had we a more intimate knowledge of that wonderful congeries of ganglia and connecting nerve filaments, the solar plexus and its associated systems, — wisely called by the ancients *cerebrum abdominale*, — we might often avert or control what is now unexpected, disastrous, or inexplicable in the operation of our more powerful remedies.

With this we must leave what for lack of a better name we call idiopathic idiosyncrasy; there is also what Mialhe has happily designated a *chemical idiosyncrasy*, due to "difference in composition of the animal fluids." The very opposite behavior of subnitrate of bismuth was for a long time a problem with therapeutists. Usually producing the local sedation for which it was given, it would occasionally be speedily followed by violent irritation and even inflammation of stomach and intestines. The theory that such action was due to admixture of arsenic did not abide results of investigation; but it was not until attention was directed to the varying reaction of the gastric mucus that the mystery received explanation. An excessive quantity of acid present in the stomach is capable of causing the conversion of the "intrinsically harmless basic salt into the corrosive neutral body; or, in consequence of the action of water upon the latter, into the poisonous acid salt."¹ These are active poisons, capable, as Orfila showed in his experiments upon animals, of producing intense gastro-enteritis.

The operation of calomel presents great variety. It has not been always safe, in my experience, to order so small a dose as one twelfth grain repeated every

¹ Lewin.

two hours; this minute quantity, so taken that the aggregate hardly exceeded one half grain, has more than once caused symptoms that simulated cholera morbus, — and this in the case of a vigorous man. Here we must suppose there is fault in the proportion of intestinal alkali and common salt. It has been observed that in patients "who have been long kept upon a low diet calomel has almost no effect, because in consequence of the excessive use of food in a liquid form the greater part of the chloride of sodium has been already washed out of the body." On the other hand, Mialhe asserts that persons who have long lived on a salty diet, as sailors, are "peculiarly sensitive to the action of calomel, and may present exceedingly intense local irritative effects in the intestines as well as a number of other unpleasant effects of mercury." Farther, Radziejewski has shown that the long-continued use of calomel may be followed by unpleasant consequences; the drug having accumulated in the cæcum, and having been then brought in contact with chloride of sodium or ammonium, is converted into corrosive sublimate, and corrosion or ulceration follows.¹

The occasional dyeing of the skin, the peculiar slaty-gray color, which may attend the continued ingestion of silver nitrate, affords a familiar illustration of chemical idiosyncrasy: perhaps there is no other instance where the measure or conditions of its determination have been established with any approach to certainty. Many authors state the time beyond which it is not safe to go, but within the limits of which the metal can

¹ That should not be imputed to chemical idiosyncrasy which, in time and place, occurs its origin, after from any contact with the patient, to the previous chemical change of the calomel through carelessness of physician or apothecary. It is well to follow the rule that the physician's calomel should be carried in a tightly-stopped vial and mixed with any other substance. Calomel may pass into the corrosive chloride in presence of the alkaline earths, this should be remembered in combination with magnesia. As is well-known, doses. Analysis of calomel pastilles, having sugar for their base, disclosed a considerable quantity of sublimate. Probably the sugar was "raw;" still it is safer to avoid sugar altogether in preparing calomel powders unless the latter are to be taken forthwith.

be used continuously with reasonable assurance of safety; and it is claimed that thirty grammes, 3vijss, is the smallest quantity of silver which has been known to produce argyria.

The patient, into whose scrotum I rubbed the oleate of mercury for swelled testicle, presented melancholy evidence of chemical idiosyncrasy for many days thereafter. I did not know that the part had been previously painted with iodine; but the mercury was not slow in discovering the fact, and a very aggressive red iodide of mercury was formed, — as it appeared, penetrating deep into the tissues, — which accomplished about the most effective and protracted counter-irritation that I ever witnessed.

Secondly. It is convenient to group together certain conditions of drug-modification under the section *Cosmic Conditions*, and, still for convenience, in this class to consider the more personal influence of habit. Whatever pertains to latitude, season, temperature, race, etc., must be glanced at in this department. Such general relation is abundantly recognized in the rude medical practice of our forefathers, whose intricate and often mystic ceremonies, both in the collection and the prescribing of their remedies, were quite possibly, in a given case, based alike upon the age of the plant, of the moon, and of the patient. Gubler insists that "cosmic conditions" should be considered in the ordering of so common a remedy as cod-liver oil; which may readily be taken in the cold of winter by the same subject who is wholly unable to continue it through hot weather on account of the disturbance which a fatty substance then occasions, both in the stomach and bowels. Lisfranc says that, of barium chloride, much larger doses are borne in warm climates than in colder regions. The great majority of lead-poisoning cases occur in the summer months, possibly because the metal is largely eliminated by the kidneys, and the functional activity of these organs, in respect of the skin, is then considerably in abeyance.

Again, ethnic conditions present a curious study for the physician. Here, clinical observation has already done somewhat for us; and, in respect of the more familiar remedies, we may know what modification of dose to make, what modification of effect to expect, when we are dealing with a pronounced type, for example, a subject of the Negro or Mongolian race. But while so much in this direction remains undetermined or obscure, we may be pardoned if we look this way for light upon certain questions which, otherwise viewed, seem hopelessly involved. The *Coca erythroylon* in its effects upon the Indian of South America, as narrated by Von Tschudi and other travelers, would appear to be the very type of a dynaphor. Under its moderate influence the body continues in a state of contented and healthful activity, although the hour for sleep has long since passed and the hour for eating has been more than once pretermitted.¹ Here would seem to be the grand corroborant for the man worn by our modern life conditions, who, out of all his food and sleep, cannot get force enough to carry him through his daily duties with any proper amount of comfort and energy.

But the result of the trial is largely a failure, though it must be acknowledged that, rarely, we get a response which encourages us to persevere with the remedy; and the disappointed practitioner turns upon the South American traveler with the charge of extravagant statement or absolute untruth. That Von Tschudi's statements are extravagant it may be allowed, but they are not thus disposed of. The historical fact remains that when the coca leaf was first introduced into Europe its marvelous effects encountered a great incredulity; they were attributed to the power of a demon, and coca had the honor of being condemned, successively, by the Jesuit fathers, by the Council of Lima, and by his Catholic

¹ Indeed, I think I have observed in my own person, in an experience of a busy hour of some pains for several years, to have before dinner, that, in addition to the usual anxiety which attends the action, the desire for food, the sense of hunger, otherwise evident, is removed for some time.

Majesty." Doubtless we seldom or never receive the drug in form calculated to display its full effects;¹ but the question is pertinent whether there may not be involved in the earlier observations a very prominent consideration of race, both as respects the aborigine and the volatile, excitable nations of Southern Europe.

Again, we are tempted to ask whether the passage of the years — of the centuries — may have introduced some material modification into the action of remedies which are now regarded as practically valueless, but which our forefathers invested with superior qualifications. Where lies the responsibility for the extraordinary change we note? Is it in the plant, or in man, or in both? Could it have been our saffron — the familiar, largely discarded saffron of the present year of grace — which so eminent a therapeutical authority as Murray extols as equivalent to "opium and wine in combination"? Must it all be ascribed to mingled superstition and ignorance, or to simple long-established prepossession, when the school of Salernum puts its often-quoted aphorism in emphatic interrogative form, How can the man die who grows sage in his garden? ("Cur moriatur homo cui crescitur salvia in horto?") Can this *salutary* sage be nothing more than the *Salvia officinalis* of to-day, more valued in culinary than in medical art?

The modifications occasioned by *habit* are so great that it is not too much to say of the man who, from long habituation as to alcohol, to opium, finds himself literally bound to continue in his accustomed indulgence, — it is not too much to say of him that he is a *changed man*; so changed in certain physical conditions, and it may well be in moral nature also, that it is well-nigh hopeless that he should be comprehended. The friend who, from interest, duty, affection, should extend the help-

¹ The drug house of C. F. Rogers, Newton, has recently procured a specimen of coca leaf and prepared a fluid extract, the latter of which is more satisfactory to me than any pharmaceutical preparation of the drug I have yet come across. But I am satisfied, that to get the full effect, the dose should be larger than it is generally stated.

ing hand cannot understand him, does not and cannot occupy common ground with him. Hence the helplessness and mischief of much that passes for temperance reform. There would seem to be an essential element in all these cases, as Lewin has pointed out, a craving for the forbidden drug, as one will crave common salt, after long abstinence from it; "just as this, an essential constituent of the body, must be supplied, so has the drug from its habitual use become an integral element for certain organs, and its omission is resented in the same way as would be that of any other elementary constituent of the body." But in an important sense *not "in the same way:"* the man who is starved for his food is a wretched sufferer, doubtless; the habitué who is starved for his opium endures a wretchedness which, fortunately, common human experience knows nothing of.

Again, a drug habit will modify the action of other toxics; thus alcohol acts badly with one accustomed to chloral hydrate, and *vice versa*.

A very singular experience is occasionally presented by both the votary of tea and of tobacco, which must probably be referred to the conjoined influence of habit and idiosyncrasy, a fact well-nigh unparalleled in what we observe of the action of other neurotics, although arsenic, in continued medicinal use, may illustrate remotely the same principle. Says Professor Hutchinson: "A man who has drunk tea all his life, and largely, may rather suddenly find that it is almost poisonous to him." So also tobacco with an individual who has used it, it may be, "without any excess, and who has been for a long time thoroughly habituated to it," may all at once begin to act as a poison without causing any distaste or any conspicuous derangement. These subjects are often quite unaware of what it is that is hurting them. They lose appetite and become nervous, and among the most conspicuous symptoms is a very marked failure of sight." There is reason for belief, by the way, that this tobacco amaurosis is most likely

to appear in such as originally presented an especially marked idiosyncrasy against tobacco, and in whom the struggle was especially severe and long before the system could be brought to receive it without protest.

Thirdly. Respecting the modifications which *age* introduces into medicinal action, space can be allowed for but brief illustration. Viewed from this stand-point, it would be difficult to find a greater contrast, throughout the entire range of commonly used medical substances, when prescribed to the young, than is presented by two narcotics which generally stand side by side in our classifications, namely, opium and belladonna. For, while the extreme type of susceptibility to the former is invariably presented by the infant, the extreme type of susceptibility to belladonna may well be found in the adult, provided it be a female of a certain temperament and physique. Again, children are but little susceptible to the toxic effects of quinia; indeed, some of Briquet's experiments would seem to show that they are capable of making a firmer stand against massive doses than adults even. *Per contra*, strychnia should be used, if prescribed to the young subject, with extreme caution. A number of severe and fatal cases of poisoning are on record from its use, hypodermically exhibited, as against paralysis sequential to diphtheria. Now farther investigation may lead to a modification of present views, but there is certainly much support for the position that the sympathetic nervous system is about equally susceptible to response in the young and adult. Materials which exert their chief physiological impression upon the body through the sympathetic — as belladonna does largely and quinia almost altogether — will be but little modified by the age of the subject, at least short of senility. Whereas materials which act primarily and chiefly through the cerebro-spinal axis, as does opium on its upper portion and strychnia on its lower tract, must, if

given to the young, be closely watched and directed with great caution.¹

In old age this principle must be differently interpreted, at least to an extent. The aged do not bear quinia well, and the remedy should be used with care. The operation of narcotics generally upon the aged has not received the attention it deserves; hyoseyanus, especially, so innocent with young children, should hardly be used at all on account of its tendency to produce a peculiar kind of mental aberration; a question not of the sympathetic, as we might have assumed, but of the brain. Chalybeates are measurably contra-indicated, so are emphatically saline cathartics. So are, to an extent, remedies which act upon the vaso-motor system, and whose influence is conditioned upon the production of a modification of calibre of arterioles and capillaries, as in the case of chloral hydrate and the bromides.

The relation of remedies to increased arterial tension is a fact of quite constant consideration with the aged. The small dose of digitalis, to energize cardiac contraction, may be opportune and beneficent in action; a few drops too much, increasing the stringency of the already too terse arteriole, may be equally disastrous. Herein probably lies an explanation of the intolerance of the aged for the larger doses of quinine, — and of ergot as well, — their physiological influence upon the heart and circulation presenting analogy with that of digitalis. Still again, hereby is explained and justified the popular repute of sweet spirits of nitre in old age,

¹ I cannot, however, agree with Albertini, who goes altogether too far in his statement that "children of fifteen months to five years of age may take, with impunity, doses of belladonna which would give rise to many symptoms of poisoning in adults." Only recently I had the unfortunate occasion to alarm a mother for whose babe, at six months, I had ordered bellad. tincture five grains of the fluid oz. Four drops, three repeated in the course of twelve hours, produced a general rash over the entire body, with inflammation of the pupils, and a considerable degree of prostration, alternating with something like stupor. That children will bear belladonna as well as adults is as much as it is safe to assume.

possibly greater in England than in this country; Dr. Leach having shown that the influence of this mild and widely applicable remedy is procured through its power to relax arterial tension, — this by virtue of its nitrous acid, an ingredient and an influence which it possesses in common with nitro-glycerine, nitrite of amyl, and nitrite of sodium, — an influence greatly to be desired in the fever, and in the arrested skin or kidney function, of the aged subject.

Much of ingenious philosophizing has been devoted by certain writers, who are in love with the theory rather than the practice of therapeutics, to the problem presented by the great variety of modifications which infancy introduces into the action of medicine. I do not know that it has occurred to any one to apply to this question the philosophy of Asclepiades. And I have sometimes wondered, by the way, — if a momentary diversion may be pardoned, — that some shrewd speculator in measures calculated to relieve those who suffer from the ills that flesh is heir to, observing the present craze of the community for the monstrous and the absurd in medicine, with whom the *omne ignotum pro magifico* of homœopathy is an unfailing source of marvel and satisfaction; I have wondered that some such mountebank has not thought to erect a system of therapeutical statics and dynamics upon the cardinal principle of Asclepiades. For Asclepiades, although the author of the proverbial wisdom which we often quote, “*cito, tuto ut jucunde*,” although the friend of Cicero, who speaks of him in his oration *De Oratore* as his personal friend and praises his skill in physic, was yet, in many things, a not unworthy predecessor of Hahnemann. Like Hahnemann, he affected to be wiser than, and to ridicule, all the fathers of medicine; and like Hahnemann he constructed his entire practice upon a preposterous proposition. — the one as preposterous in pathology as the other in therapeutics; both alike as captivating in the sound, to the untrained at least, as misleading in the sense, — to wit, that *all disease is due to obstruction*

of the primary atoms in their passage through the invisible pores. This might serve us well in removing the difficulties of our present question, — if anything could be expected of remedies in such narrow and exiguous conflict, — for surely in infancy the atoms must be particularly “primary” and the pores particularly “invisible.”

It were to be wished there was time to consider, practically, the modifications occasioned by infancy in the action of three prominent drugs, namely, opium, antimony, and mercury. Dr. Beck is the only authority, so far as I know, who has thought it worth while to write upon this subject, and his monograph was published some years ago. And yet this is a matter of very great concern to every practitioner. As respects opium, the young physician, unless he have some other guide than text-books and lecture-courses afford, and unless he be a man of exceptional caution, is in danger of gaining his early information through fatal experience. I can remember several young children that I believe I nearly killed by opium in the first years of my practice, and I went by the books. The fact that this drug acts upon the upper part of the spinal cord, below the brain, in the very young, when the inhibitory power of the brain over this portion of the nerve tract is at its minimum, and the fact, which Seguin appears to have established, that the “convulsibility” of the spinal cord ceases at about three years of age, suggest the importance of avoiding opium, so far as we may, till the child has passed this age.

Some one has said that the words *never* and *always* should not be used in connection with any medical subject. If there be an exception to this rule I think we have found it when we insist that *antimony should always be avoided, should never be used, in treating the very young.* Ipecac will do almost or quite as well, and ipecac is wholly safe. A prominent English writer, whose name I do not recall, writing ten to fifteen years ago, suggests as explanatory of the much greater fa-

talities of croup in rural districts than in London the so much freer use by the country practitioner of antimony in treating the disease. It will be admitted that this drug is not as much used as formerly, but it is still employed altogether too much, that is, with the infant. Again, we insist our remarks are pertinent when it is remembered how commonly and freely the seductive "hive syrup" is still used in domestic practice, often with entire unconsciousness, even on the part of intelligent families, of its composition and its power.

Fourthly. The modification which may take place in a remedy by the *contemporaneous operation of another drug*, once fairly considered, would lead us to the discussion of combination, antagonism, etc., and all this, of course, must be set aside. A recent astute writer has well observed that there are few facts of pharmacodynamics, as, indeed, of practical therapeutics, of equal importance with that which has to do with the elimination of a medicine, adding that the old aphorism "*non agunt nisi soluta*" should rather read *non agunt nisi secreta*. Gubler has applied the term *vector* to a material which diverts another material from its usual avenue of elimination. Iodine, and probably bromine also, in combination with iron, is an illustration of the vector, the metal in this form or companionship being carried to the salivary glands, at least in a measure, a direction which no other chalybeate has been observed to take. Camphor is not eliminated by the kidneys, and would seem to have the power of carrying with itself, away from the kidneys, cantharides, which, otherwise, would seek this avenue of egress from the system; hence the influence of camphor as an antidote. "Camphor, in whatever doses taken by the stomach, is never passed in the urine" (Gubler), but monobromated camphor leaves the body by the kidneys, the bromine serving as vector.

Fifthly. The modifications impressed upon the action of a prominent material, for example, quinia or opium, according as the influence exerted is *physiolog-*

ical or therapeutical, are more or less familiar to every tyro in medicine. Thus the most innocent substance can be converted for the occasion into the most lethal, as iron in certain states of disease. *Per contra*, the most powerful alterative becomes an emphatic tonic, corroborant, restorative; and if that which, at all other times, is a most potent and a universal disorganizer, does not directly serve in the rôle of hæmato-sis and histogenesis, it does certainly stand as the essential vital catalytic, the *sine qua non*, without whose interposition these processes cannot, to the best estate, be resumed and continued. All this we observe of mercury in a certain stage of syphilis.

Every physician is familiar with the difference between the physiological and therapeutical action of alcohol. I have known a delicate woman, suddenly exsanguinated, consume a bottle of brandy in the course of a single night, and never once, as the saying is, feel it in her head; and yet, from previous experience, she could not probably have told the difference between cognac and sherry. Suddenly produced anæmia is one of the three conditions, — anæmia, spasm, pain, — and first among the three, which renders safe and beneficial large doses of opium; we have therapeutical for toxic impression, as in the teaspoonful doses of laudanum and upwards ordered by Gough and Hamilton in puerperal hæmorrhage.

An incident related in a sketch of the life of the late eminent orientalist and hero, Edward Henry Palmer, illustrates the principle, now being considered, in respect of alcohol. "One night, in 1865, he fell back on the sofa, and lay resting on his head and heels. The case closely resembled tetanus. Gradually he came round, and for months afterwards was compelled to drink enormous quantities of brandy, which produced no more effect on him than so much water. One night he was in the rooms of a man who produced a bottle of whiskey. Palmer drank a glass of hot whiskey and water, and then leaned over and whispered to a friend,

‘Take me away at once or I shall begin to talk about my rich uncles.’ When he reached the bottom of the stairs he was so drunk he could not stand. ‘You never before,’ he said next day, ‘saw a man who did right in thanking God that he was drunk. I was drunk last night, and now I know that I am quite well again.’ There was no more drinking of brandy.”

All that we know of the physiological action of the remedy would lead us to say that iodine never kills unless given with intent to kill or through ignorance or carelessness, equally culpable; and yet a brief course of iodine has been known to cause death. “True œdema of the glottis, as has been proven by the observations of Petitjean, may be produced by medicinal doses of iodide of potassium, *but only* in persons suffering from laryngeal affections before receiving the drug.”¹ Here, through modification brought about by topical disease, the otherwise harmless and slight catarrh of the larynx, always liable to attend the physiological action of iodine, is magnified into a condition capable of causing speedy asphyxia.

Again, medicines may stand closely together as respects their physiological manifestations which have little in common when applied as remedies; physiologically nearly allied, therapeutically they touch at very few points or not at all. The phenomena of cinchonism and iodism are singularly alike, but cinchona belongs to the class of tonics, and iodine to the class of alteratives, while their medicinal indications are widely different. The physiological influence of ergot, digitalis, and quinia, as brought to bear upon the heart, stomach, and cerebral circulation, presents striking analogies, but not such as can be safely followed very far in practice, and of which, indeed, but little practical account can be made.

Once more, the physiological influence of a subordinate or obscure drug may tread closely upon that of a drug of the highest value, and yet the therapeutical

¹ Lewin.

power of the former be almost nil, or its range of medicinal influence very limited. Thus the excitation which follows apiol, in doses of two grammes and upwards, suggests at once the more characteristic phenomena of cinchonism as expressed by ringing in the ears, headache, titubation, and tendency to vertigo. The effluvia given forth by saffron possesses properties allied to those of the anaesthetics, producing, after a time, headache, muscular feebleness, a sort of indolence, torpor, and even stupor," etc., etc.¹ It goes without the saying that apiol would be a poor dependence in, perhaps, so much as one of the many conditions in which quinia is employed, while the aromatic odors of saffron would accomplish little towards the production of anaesthesia.

Sixthly and finally. Medicines are materially modified according to the *method and form of their use*. We have suggested changes caused (1) by the avenue through which the remedy reaches the system, (2) by its pharmaceutical status, and (3) by posology or dosage.

For a long time the constitutional effects of mercury were procured solely through inunction. It was not ventured to introduce into the interior of the body so powerful a poison. Our experience with the oleate, of the last few years, has partly revived the practice of former centuries, in less objectionable form, and assured us there was much to be said in its favor which had been long forgotten. Certain therapeutic modifications, certain wholly new resources, obtained through external and also through hypodermic exhibition, are of great value.

One fact, cautionary, respecting atomizing, and that of the cutaneous surface. "It has been proved by the investigations of Rohrig that finely pulverized, watery solutions of substances are taken up by the skin, while they are not absorbed if simply laid upon it. The experiments made upon this point, which were made

¹ Gubler.

with all possible precautions, showed that when watery solutions of the iodide or ferrocyanide of potash, for example, were applied to the skin in a finely divided condition one or the other of the drugs appeared in the urine. Animals could also be stupefied or brought into a paralytic condition by solutions of morphia or woorara exhibited in the same manner. This proves that the act of atomizing introduces substances into the body much more readily and in larger quantities than simple contact. Therefore the belief is fully justified that a very large portion of carbolic acid, employed in the form of spray, is absorbed by the skin or its sweat glands."¹ Such poisoning would be especially liable to obtain with children, who "naturally possess a much more limited power of resistance, since the surface of the skin occupied by the spray is much larger, in proportion to the whole surface of the body, than in adults, and, therefore, *cet. par.*, much more carbolic acid is taken into the system."

As respects modifications in medicinal action through rectal insertion there is need of farther research. We have at least corrected certain of the errors in vogue not many years ago. It has been proved that oils may be absorbed from this cavity, although this was, not long since, almost universally denied. We have repudiated the former false ratio which determined that the dose of opium, *per rectum*, should be three-fold that *per os*. It may well be that children have been killed *secundum artem* by obedience to this rash tenet. Certain authorities, and Briquet prominently, assert of quinia that the dose by the rectum should be relatively small, as the activity of the remedy is relatively greater thus administered.

Space remains but for a remark concerning posologic modification, the contrast, to wit, always to be observed between the physiological and the toxic impression of any powerful remedy. This suggests allusion to the not infrequent charge, brought by the ignorant

¹ Lewin.

or prejudiced against physicians that they prescribe poisons for their patients; such triflers as amuse themselves with the inert inanities of homoeopathy escaping this condemnation, and to them, in the present mood of the community, "it makes for righteousness." For although prepossession may expect some virtue from "*arsenicum*" or "*mercurius*," yet a very small modicum of common sense is prompt to declare that they can do no harm.

Now, gentlemen, it should be understood and insisted upon that we never prescribe poisons. We use morphia, strychnia, atropia as occasion calls, but we do not exhibit them in poisonous dose; they do not exert a poisonous action; they are not poisonous agents in our hands. There is as much difference — nay, there is more — in the operation of aconite as a remedy and aconite as a poison as there is in the toxic operation of aconite and digitalis, or the toxic operation of opium and nux vomica, of arsenic and mercury.

